REMARKS

Claims 1-5, 7-9, and 16-19 were pending in the subject application. Claims 6, 10-15, and 20-26 were withdrawn. Applicants hereinabove have cancelled claims 6, 10-15, and 20-26, amended claim 16, and added new claims 27-28. Accordingly, claims 1-5, 7-9, 16-19, and 27-28 are pending and under examination in the subject application.

New claims 27-28 depend from amended claim 16, which is believed to fall within Group I, the Group provisionally elected by applicants in their July 16, 2003 response to June 16, 2003 Office Action. New claims 27-28 recite the same subject matter as claims 1, 16, and cancelled claim 14. Accordingly, support for new claims 27-28 may be found inter alia in the portions of the specification that support claims 1, 16, and cancelled claim 14.

Applicants hereinabove have amended the specification by adding a new first paragraph, which recites the instant application's chain of priority. The new first paragraph specifically refers to International Application No. PCT/US00/01957, filed January 25, 2000, from which the instant application claims the benefit of priority. This priority claim was made on page one of the transmittal letter which accompanied the instant application when filed on July 25, 2001 **(Exhibit A)**. International Application No. PCT/US00/01957 in turn claims the benefit of U.S. Provisional Application No. 60/117,099, filed January 25, 1999. This priority claim was made in Box No. VI of the first sheet of the original PCT Request **(Exhibit B)**. Accordingly, this Amendment raises no issue of new matter, and applicants respectfully request that it be entered.

Rejections under 35 U.S.C. § 102(a)

On page 4 of the November 14, 2003 Office Action, the Examiner rejected claims 1, 5, and 16-19 under 35 U.S.C. §102(a) as allegedly being anticipated by Tamilarasu et al., *J. Am. Chem. Soc.* **1999**, *121*, 1597. The Examiner alleged that Tamilarasu et al. discloses the preparation of Tat-derived oligoureas and meets all of the claimed limitations.

In response, applicants traverse the rejection and respectfully point out to the Examiner that a rejection under 35 U.S.C. §102(a) requires inter alia that the invention be described by *others* in a printed publication (italics supplied). Applicants note that the inventors of the subject application, namely Rana, Tamilarasu, and Huq, are also the same three authors of the above-indicated *J. Am. Chem. Soc.* publication. Applicants have attached as **Exhibit C** a copy of the declarations filed with the U.S. Patent and Trademark Office on November 21, 1999, indicating their inventorship of the subject invention.

Accordingly, applicants respectfully request that the Examiner reconsider and withdraw this rejection of claims 1, 5, and 16-19.

Rejections under 35 U.S.C. §102(e)

On page 3 of the November 14, 2003 Office Action, the Examiner rejected claims 1-5, 7-9, and 16-19 under 35 U.S.C. §102(e) as purportedly being anticipated by Rana et al., U.S. Patent No. 6,583,309 B1. The Examiner alleged that Rana and colleagues disclose the preparation of TAT-derived oligoureas and their utilization to inhibit TAT activities. The Examiner specifically pointed out columns 39, 40, and 48-52 of the '309 patent. The Examiner further alleged that the teaching meets all of the claimed limitations of the subject application.

In response, applicants traverse the rejection and respectfully point out to the Examiner that a rejection under 35 U.S.C. §102(e) requires inter alia that the invention by others be "patented or described in a printed publication... *before* the invention thereof by the applicant for patent." Applicants note that the subject application is a 35 U.S.C. §371 National Stage Application of International Application No. PCT/US00/01957, filed January 25, 2000, which claims the benefit of U.S. Provisional Application No. 60/117,099, filed January 25, 1999. The priority date of the subject application is thus January 25, 1999. The earliest effective U.S. filing

date of the '309 patent, on the other hand, is October 4, 1999, approximately eight months after the subject application's January 25, 1999 priority date.

Accordingly, applicants respectfully request that the Examiner reconsider and withdraw the rejection of claims 1-5, 7-9, and 16-19.

Rejections under 35 U.S.C. §102(f)

On page 3 of the November 14, 2003 Office Action, the Examiner rejected claims 1-5, 7-9, and 16-19 under 35 U.S.C. §102(f), alleging that applicants did not invent the claimed subject matter. The Examiner alleged that Rana et al., U.S. Patent No. 6,583,309 B1, teaches the instantly claimed invention. The Examiner noted that the '309 patent lists three inventors, including two of the inventors of the instant application. The Examiner further noted that the '309 patent also includes a third individual who is not a listed inventor in the instant application.

In response, applicants traverse the rejection and respectfully point out that the Examiner has provided no evidence to support a 102(f) rejection. The Examiner alleges that the '309 patent discloses the preparation of TAT-derived oligoureas and their utilization to inhibit TAT activities. The Examiner cited columns 39, 40, and 48-52 in support of this contention. The Examiner further alleged that this teaching meets all of the claimed limitations.

Applicants respectfully point out that the Examiner's citation fails to teach each and every element of the rejected claims. Applicants note that the '309 patent does not discuss "a synthesized oligourea comprising the basic-arginine rich region of TAT" and corresponding methods of use, as recited in applicants' claims 1-4. Neither does the '309 patent discuss a "synthesized oligourea comprising the sequence" of amino acid residues 48 to 57 of the TAT protein, and corresponding methods of use, as recited in applicants' claims 5, and 7-9. Finally, the '309 patent does not discuss a composition comprising an oligourea with amino acid side

chains corresponding in various ways to the TAT protein and its sequence of amino acids as recited in applicants' claims 16-19.

There is in fact only one reference in the '309 patent to the relevant portion of the TAT protein, and it is not presented in the context of discussing an aspect of the '309 invention. Rather, the '309 patent discusses this sequence only insofar as it is used as a means to evaluate the binding of the '309 compounds to TAR RNA (see columns 49-52 of the '309 patent). The binding of the '309 compounds was assessed by measuring their inhibition of TAR-TAT complex formation. In lieu of using the entire TAT protein, a shortened TAT peptide sequence was used in the assay: GRKKRRQRRR, i.e. amino acids 48-47 of the intact TAT protein. Binding ability of the '309 compounds was determined by measuring their inhibition of interaction of TAR RNA with this shortened TAT peptide sequence. Thus, instead of teaching this sequence of amino acids as being a component of the invention, the '309 patent mentions the sequence merely in the context of its role as a peptide against which the '309 compound competes for interaction with the TAR RNA.

As the Tat peptide sequence side-chain is neither disclosed nor taught as part of the '309 invention itself, applicants respectfully request that the Examiner reconsider and withdraw the rejection of claims 1-5, 7-9, and 16-19.

Rejections under 35 U.S.C. §112, First Paragraph

The Examiner has rejected claims 1-5, 7-9 and 16-19 under 35 U.S.C. §112, First Paragraph. Applicants request that these rejections be withdrawn on the basis that applicants' specification as filed provides adequate support, as well as working embodiments, for both *in vivo* and *ex vivo* applications.

Regarding these rejections, the Examiner states the following:

The disclosure describes the preparation of Tat-derived oligoureas and their ability to inhibit HIV-1 Tat binding to the Tar element in a suitable in vitro binding assay. Appropriately drafted claim language directed toward in vitro binding methods would be acceptable. However, the full breadth of the claims encompasses in vitro and both in vivo and ex vivo clinical applications. However, the disclosure fails to support both in vivo and ex vivo applications at this point in time.

Applicants do not agree with the Examiner's statements, which allege that the disclosure of the present application fails to provide support for anything other than *in vitro* methods. As the Examiner is aware, prior to determining whether the disclosure satisfies the written description requirement for the claimed subject matter, a review of the claims and the entire specification should be made, including the drawings. Moreover, this analysis needs to be conducted from the standpoint of one of skill in the art at the time the application was filed.

Figure 4 of the present application and the description therefore at page 5, lines 10-19, provide clear support in the disclosure for *in vivo* inhibitory methods. Figure 4 depicts a working embodiment of the invention as it pertains to *in vivo* inhibitory methods. In particular, Figure 4 depicts inhibition of Tat transactivation by an oligourea derivative of the present invention *in vivo*. A person of ordinary skill in the art would immediately recognize that applicants had possession of the claimed invention, as it applies to both *in vitro,* as well as *in vivo* applications. Transactivation assays similar to the one depicted in Figure 4, which employ reporter systems, such as CAT, have been known in the art at least as far back as the 1980's (see, for example, Miesfeld, *et al.* (1986) Cell 46: 389-399.) Suitable protocols for carrying out these assays are well known to one of ordinary skill in the art. Moreover, applicants have used well-established terms to describe the *in vivo* assay of Figure 4. Such well-established terms or procedures do not have to be described in detail in the specification and should not be the basis of a rejection, based on the Written Description Guidelines. In the present assay, HL3T1 cells, which are a HeLa derivative cell line containing an integrated HIV LTR-1 promoter and CAT reporter gene, were used. Such cells are known in the art (see, for example, Felber and Pavlakis (1988) Science 239:184-186). These cells were transfected with the plasmid pSV2Tat (an expression plasmid

that contains the Tat coding region) and increasing amounts of the oligourea of the present invention. The plasmid pSV2Tat is also known in the art (Helland, et al. (1991) J. Virol. 65:4547-4549; and Bonifaci, Sitia and Rubartelli (1995) AIDS 9:995-1000). Luciferase was introduced (encoded by a plasmid), along with the expression plasmid and the oligourea compound, as a reference to normalize for transfection efficiency. Similar *in vivo* assays with different oligourea compounds have also been described in commonly-owned U.S. Patent No. 6,583,309 B1 at column 50, lines 18-40. Figure 4 of the present application shows CAT activity expressed from the integrated HIV-1 LTR of the HL3T1 cells with increasing amounts of an oligourea derivative according to the present invention, as compared to in the absence of the oligourea derivative. The results indicate that an oligourea of the present invention inhibits Tat transactivation. Since Tat transactivation requires the interaction of the trans-activation responsive region (TAR) RNA with the specific binding protein Tat, the oligourea can be said to have inhibited this interaction (i.e., binding) when it was introduced into a cellular environment wherein the inhibition was sought to occur. Therefore, applicants have provided a working example of an *in vivo* inhibitory method, as defined in applicants' claims.

The Examiner also alleges that the prior art teaches that the generation of successful HIV-1 antivirals is a difficult and unpredictable process. The Examiner states the following:

> **Several factors have contributed to antiviral failure including short serum half-lives, poor bioavailabilities, rapid clearance rates, sequestration of the drug by serum proteins, drug resistance to the quasispecies nature of HIV-1 infection, and the uneven distribution of the compound throughout the body (Gait et al., 1995). The disclosure fails to address any of these concerns.**

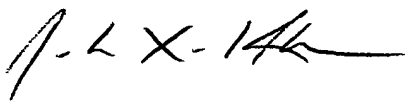
Applicants do not agree with the Examiner's allegations. The Examiner has recognized applicants' support for *in vitro* binding assays. Furthermore, applicants provide clear support in the disclosure for *in vivo* inhibitory methods, as well as working embodiments as they pertain to *in vivo* and *in vitro* applications. In particular, the *in vivo* assay depicted in applicants' Figure 4, shows the oligourea compound operating in a cellular environment reflective of the milieu where such compounds would be required to operate. Moreover, applicants specification teaches that

oligourea compounds of the present invention bind specifically to TAR RNA with high affinities (page 10, lines 9-14; page 11, lines 20-25) and form oligourea-RNA complexes which are stable when subjected to alkaline pH, high temperature, denaturing conditions, and protease digestion (page 12, lines 24-35; page 13, lines 1-11) -all desirable pharmacokinetic properties. Furthermore, as the Examiner is aware, applicants are not required to provide evidence of actual success in treating humans or animals for patentability. The requirements under the law for obtaining a patent should not be confused with the requirements for obtaining governmental approval to market a particular drug for human consumption.

In view of these remarks, applicants respectfully request that the Examiner withdraw the rejections under 35 U.S.C. §112, First Paragraph.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.

Respectfully submitted,



John X. Haberman
Registration No. 55,236
Attorney for Applicants

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(973) 331-1700

Docket No.: 13257-00018
In re application of

UMDNJ

Serial No N/A
Filing Date: Herewith

: Date: 25 July 2001
: The following items were received by the PTO:
:
: PTO 1390
: Express Mail Certificate
: Check
: Postcard Receipt

For: Biopolymers Comprising Human Immunodeficiency Virus TAT

****

The PTO is respectfully requested to place its STAMP on the POSTAL CARD and place it in the outgoing mail.

Janet E. Reed
Reg. No. 36,252

09/889982

609718.1 7/24/01

500 Rec'd PCT/PTO 25 JUL 2001

FORM PTO-1390 (REV. 11-2000) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371

ATTORNEY'S DOCKET NUMBER: 13257-00018

U.S. APPLICATION NO. (If known, see 37 CFR 1.5):

INTERNATIONAL APPLICATION NO.	INTERNATIONAL FILING DATE	PRIORITY DATE CLAIMED
PCT/US00/01957	25 January 2000 (25.01.00)	25 January 1999 (25.01.99)

TITLE OF INVENTION: Biopolymers Comprisihng Human Immunodeficiency Virus Tat

APPLICANT(S) FOR DO/EO/US: RANA, Tariq M.

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. [X] This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. [ ] This is a **SECOND or SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. [ ] This is an express request to begin national examination procedures (35 U.S.C. 371(f)). The submission must include items (5), (6), (9) and (21) indicated below.
4. [ ] The US has been elected by the expiration of 19 months from the priority date (Article 31).
5. [X] A copy of the International Application as filed (35 U.S.C. 371(c)(2))
   a. [ ] is attached hereto (required only if not communicated by the International Bureau).
   b. [ ] has been communicated by the International Bureau.
   c. [X] is not required, as the application was filed in the United States Receiving Office (RO/US).
6. [ ] An English language translation of the International Application as filed (35 U.S.C. 371(c)(2)).
   a. [ ] is attached hereto.
   b. [ ] has been previously submitted under 35 U.S.C. 154(d)(4).
7. [X] Amendments to the claims of the International Aplication under PCT Article 19 (35 U.S.C. 371(c)(3))
   a. [ ] are attached hereto (required only if not communicated by the International Bureau).
   b. [ ] have been communicated by the International Bureau.
   c. [ ] have not been made; however, the time limit for making such amendments has NOT expired.
   d. [X] have not been made and will not be made.
8. [ ] An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371 (c)(3)).
9. [ ] An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).
10. [ ] An English lanugage translation of the annexes of the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

Items 11 to 20 below concern document(s) or information included:

11. [ ] An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
12. [ ] An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
13. [ ] A FIRST preliminary amendment.
14. [ ] A SECOND or SUBSEQUENT preliminary amendment.
15. [ ] A substitute specification.
16. [ ] A change of power of attorney and/or address letter.
17. [ ] A computer-readable form of the sequence listing in accordance with PCT Rule 13ter.2 and 35 U.S.C. 1.821 - 1.825.
18. [ ] A second copy of the published international application under 35 U.S.C. 154(d)(4).
19. [ ] A second copy of the English language translation of the international application under 35 U.S.C. 154(d)(4).
20. [ ] Other items or information:

U.S. APPLICATION NO. (if known, see 37 CFR 1.5)	INTERNATIONAL APPLICATION NO.	ATTORNEY'S DOCKET NUMBER
	PCT/US00/01957	13257-00018

21. ☒ The following fees are submitted:

BASIC NATIONAL FEE (37 CFR 1.492 (a) (1) - (5)):

		CALCULATIONS PTO USE ONLY
Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a (2)) paid to USPTO and International Search Report not prepared by the EPO or JPO	$1000.00	
International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO	$860.00	
International preliminary examination fee (37 CFR 1.482) not paid to USPTO but international search fee (37 CFR 1.445(a)(2)) paid to USPTO	$710.00	
International preliminary examination fee (37 CFR 1.482) paid to USPTO but all claims did not satisfy provisions of PCT Article 33(1)-(4)	$690.00	
International preliminary examination fee (37 CFR 1.482) paid to USPTO and all claims satisfied provisions of PCT Article 33(1)-(4)	$100.00	
ENTER APPROPRIATE BASIC FEE AMOUNT =		$ 100.00
Surcharge of $130.00 for furnishing the oath or declaration later than ☐ 20 ☐ 30 months from the earliest claimed priority date (37 CFR 1.492(e)).		$

CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE	
Total claims	26 -20 =	6	x $18.00	$ 108.00
Independent claims	4 -3 =	1	x $80.00	$ 80.00
MULTIPLE DEPENDENT CLAIM(S) (if applicable)			+ $270.00	$ 0.00

TOTAL OF ABOVE CALCULATIONS =	$
☐ Applicant claims small entity status. See 37 CFR 1.27. The fees indicated above are reduced by 1/2. +	$ 0.00
SUBTOTAL =	$
Processing fee of $130.00 for furnishing the English translation later than ☐ 20 ☐ 30 months from the earliest claimed priority date (37 CFR 1.492(f)).	$
TOTAL NATIONAL FEE =	$
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). $40.00 per property +	$ 188.00
TOTAL FEES ENCLOSED =	$
Amount to be refunded:	$
charged:	$

a. ☒ A check in the amount of $ 188.00 to cover the above fees is enclosed.

b. ☐ Please charge my Deposit Account No. _____ in the amount of $ _____ to cover the above fees. A duplicate copy of this sheet is enclosed.

c. ☒ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 50-1089. A duplicate copy of this sheet is enclosed.

d. ☐ Fees are to be charged to a credit card. **WARNING:** Information on this form may become public. **Credit card information should not be included on this form.** Provide credit card information and authorization on PTO-2038.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137 (a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:

Janet E. Reed
Saul Ewing
1500 Market Street, 38th Floor
Centre Square Building West
Philadelphia, PA 19102

Janet E. Reed
SIGNATURE

Janet E. Reed
NAME

36,252
REGISTRATION NUMBER

PCT

REQUEST

The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty.

For receiving Office use only

International Application No.

International Filing Date

Name of receiving Office and "PCT International Application"

Applicant's or agent's file reference *(if desired) (12 characters maximum)* UMDNJ RWJ 99-02

Box No. I TITLE OF INVENTION

TAT-DERIVED OLIGOUREA AND ITS METHOD OF PRODUCTION AND USE IN HIGH AFFINITY AND SPECIFIC BINDING OF HIV-1 TAR RNA

Box No. II APPLICANT

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

UNIVERSITY OF MEDICINE AND DENTISTRY OF NEW JERSEY
335 George Street
Suite 3200
New Brunswick, New Jersey 08903-2688
United States of America

☐ This person is also inventor.

Telephone No. (732) 235-9350

Facsimile No. (732) 235-9358

Teleprinter No.

State *(that is, country)* of nationality: United States of America

State *(that is, country)* of residence: United States of America

This person is applicant for the purposes of: ☐ all designated States ☒ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

RANA, Tariq M.
22 Johanna Court
Piscataway, New Jersey 08854
United States of America

This person is:

☐ applicant only

☒ applicant and inventor

☐ inventor only *(If this check-box is marked, do not fill in below.)*

State *(that is, country)* of nationality: United States of America

State *(that is, country)* of residence: United States of America

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☒ the United States of America only ☐ the States indicated in the Supplemental Box

☐ Further applicants and/or (further) inventors are indicated on a continuation sheet.

Box No. IV AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE

The person identified below is hereby/has been appointed to act on behalf of the applicant(s) before the competent International Authorities as: ☒ agent ☐ common representative

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

KLANN, Ellen M.
DANN, DORFMAN, HERRELL AND SKILLMAN
1601 Market Street
Suite 720
Philadelphia, Pennsylvania 19103
United States of America

Telephone No. (215) 563-4100

Facsimile No. (215) 563-4044

Teleprinter No.

☐ **Address for correspondence:** Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.

Box No.V DESIGNATION OF STATES

The following designations are hereby made under Rule 4.9(a) *(mark the applicable check-boxes; at least one must be marked)*:

Regional Patent

☐ **AP** **ARIPO Patent:** GH Ghana, GM Gambia, KE Kenya, LS Lesotho, MW Malawi, SD Sudan, SL Sierra Leone, SZ Swaziland, TZ United Republic of Tanzania, UG Uganda, ZW Zimbabwe, and any other State which is a Contracting State of the Harare Protocol and of the PCT

☐ **EA** **Eurasian Patent:** AM Armenia, AZ Azerbaijan, BY Belarus, KG Kyrgyzstan, KZ Kazakhstan, MD Republic of Moldova, RU Russian Federation, TJ Tajikistan, TM Turkmenistan, and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT

☒ **EP** **European Patent:** AT Austria, BE Belgium, CH and LI Switzerland and Liechtenstein, CY Cyprus, DE Germany, DK Denmark, ES Spain, FI Finland, FR France, GB United Kingdom, GR Greece, IE Ireland, IT Italy, LU Luxembourg, MC Monaco, NL Netherlands, PT Portugal, SE Sweden, and any other State which is a Contracting State of the European Patent Convention and of the PCT

☐ **OA** **OAPI Patent:** BF Burkina Faso, BJ Benin, CF Central African Republic, CG Congo, CI Côte d'Ivoire, CM Cameroon, GA Gabon, GN Guinea, GW Guinea-Bissau, ML Mali, MR Mauritania, NE Niger, SN Senegal, TD Chad, TG Togo, and any other State which is a member State of OAPI and a Contracting State of the PCT *(if other kind of protection or treatment desired, specify on dotted line)* .....

National Patent *(if other kind of protection or treatment desired, specify on dotted line)*:

☐ **AE** United Arab Emirates
☐ **AL** Albania .....
☐ **AM** Armenia .....
☐ **AT** Austria .....
☒ **AU** Australia .....
☐ **AZ** Azerbaijan
☐ **BA** Bosnia and Herzegovina .....
☐ **BB** Barbados
☐ **BG** Bulgaria .....
☐ **BR** Brazil .....
☐ **BY** Belarus .....
☒ **CA** Canada
☐ **CH and LI** Switzerland and Liechtenstein
☐ **CN** China .....
☐ **CR** Costa Rica .....
☐ **CU** Cuba .....
☐ **CZ** Czech Republic .....
☐ **DE** Germany .....
☐ **DK** Denmark .....
☐ **DM** Dominica
☐ **EE** Estonia .....
☐ **ES** Spain .....
☐ **FI** Finland .....
☐ **GB** United Kingdom
☐ **GD** Grenada
☐ **GE** Georgia .....
☐ **GH** Ghana .....
☐ **GM** Gambia
☐ **HR** Croatia .....
☐ **HU** Hungary .....
☐ **ID** Indonesia
☐ **IL** Israel .....
☐ **IN** India .....
☐ **IS** Iceland
☒ **JP** Japan .....
☐ **KE** Kenya .....
☐ **KG** Kyrgyzstan .....
☐ **KP** Democratic People's Republic of Korea .....
☐ **KR** Republic of Korea .....
☐ **KZ** Kazakhstan .....
☐ **LC** Saint Lucia
☐ **LK** Sri Lanka
☐ **LR** Liberia
☐ **LS** Lesotho .....
☐ **LT** Lithuania
☐ **LU** Luxembourg
☐ **LV** Latvia
☐ **MA** Morocco .....
☐ **MD** Republic of Moldova .....
☐ **MG** Madagascar .....
☐ **MK** The former Yugoslav Republic of Macedonia .....
☐ **MN** Mongolia
☐ **MW** Malawi .....
☐ **MX** Mexico .....
☐ **NO** Norway
☐ **NZ** New Zealand .....
☐ **PL** Poland .....
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☐ **RO** Romania
☐ **RU** Russian Federation .....
☐ **SD** Sudan
☐ **SE** Sweden
☐ **SG** Singapore
☐ **SI** Slovenia .....
☐ **SK** Slovakia .....
☐ **SL** Sierra Leone .....
☐ **TJ** Tajikistan .....
☐ **TM** Turkmenistan .....
☐ **TR** Turkey .....
☐ **TT** Trinidad and Tobago .....
☐ **TZ** United Republic of Tanzania
☐ **UA** Ukraine .....
☐ **UG** Uganda .....
☒ **US** United States of America .....
☐ **UZ** Uzbekistan .....
☐ **VN** Viet Nam .....
☐ **YU** Yugoslavia .....
☐ **ZA** South Africa .....
☐ **ZW** Zimbabwe .....

Check-boxes reserved for designating States which have become party to the PCT after issuance of this sheet:

☐ .....
☐ .....

Precautionary Designation Statement: In addition to the designations made above, the applicant also makes under Rule 4.9(b) all other designations which would be permitted under the PCT except any designation(s) indicated in the Supplemental Box as being excluded from the scope of this statement. The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. *(Confirmation (including fees) must reach the receiving Office within the 15-month time limit.)*

See Notes to the request form

Supplemental Box *If the Supplemental Box is not used, this sheet should not be included with the request.*

1. If, in any of the Boxes, the space is insufficient to furnish all the information: in such case, write "Continuation of Box No. ..." [indicate the number of the Box] and furnish the information in the same manner as required according to the captions of the Box in which the space was insufficient, in particular:

(i) if more than two persons are involved as applicants and/or inventors and no "continuation sheet" is available: in such case, write "Continuation of Box No. III" and indicate for each additional person the same type of information as required in Box No. III. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below;

(ii) if, in Box No. II or in any of the sub-boxes of Box No. III, the indication "the States indicated in the Supplemental Box" is checked: in such case, write "Continuation of Box No. II" or "Continuation of Box No. III" or "Continuation of Boxes No. II and No. III" (as the case may be), indicate the name of the applicant(s) involved and, next to (each) such name, the State(s) (and/or, where applicable, ARIPO, Eurasian, European or OAPI patent) for the purposes of which the named person is applicant;

(iii) if, in Box No. II or in any of the sub-boxes of Box No. III, the inventor or the inventor/applicant is not inventor for the purposes of all designated States or for the purposes of the United States of America: in such case, write "Continuation of Box No. II" or "Continuation of Box No. III" or "Continuation of Boxes No. II and No. III" (as the case may be), indicate the name of the inventor(s) and, next to (each) such name, the State(s) (and/or, where applicable, ARIPO, Eurasian, European or OAPI patent) for the purposes of which the named person is inventor;

(iv) if, in addition to the agent(s) indicated in Box No. IV, there are further agents: in such case, write "Continuation of Box No. IV" and indicate for each further agent the same type of information as required in Box No. IV;

(v) if, in Box No. V, the name of any State (or OAPI) is accompanied by the indication "patent of addition," or "certificate of addition," or if, in Box No. V, the name of the United States of America is accompanied by an indication "continuation" or "continuation-in-part": in such case, write "Continuation of Box No. V" and the name of each State involved (or OAPI), and after the name of each such State (or OAPI), the number of the parent title or parent application and the date of grant of the parent title or filing of the parent application;

(vi) if, in Box No. VI, there are more than three earlier applications whose priority is claimed: in such case, write "Continuation of Box No. VI" and indicate for each additional earlier application the same type of information as required in Box No. VI;

(vii) if, in Box No. VI, the earlier application is an ARIPO application: in such case, write "Continuation of Box No. VI", specify the number of the item corresponding to that earlier application and indicate at least one country party to the Paris Convention for the Protection of Industrial Property for which that earlier application was filed.

2. If, with regard to the precautionary designation statement contained in Box No. V, the applicant wishes to exclude any State(s) from the scope of that statement: in such case, write "Designation(s) excluded from precautionary designation statement" and indicate the name or two-letter code of each State so excluded.

3. If the applicant claims, in respect of any designated Office, the benefits of provisions of the national law concerning non-prejudicial disclosures or exceptions to lack of novelty: in such case, write "Statement concerning non-prejudicial disclosures or exceptions to lack of novelty" and furnish that statement below.

CONTINUATION OF BOX IV

DORFMAN, John C.
HERRELL, Roger W.
SKILLMAN, Henry H.
PIPER, Jr., Donald R.
PACE, Vincent T.
HAGAN, Patrick J.
REED, Janet E.

All above attorneys are of the firm of DANN, DORFMAN, HERRELL AND SKILLMAN.
Address of all is indicated in Box IV.

Box No. VI PRIORITY CLAIM ☐ Further priority claims are indicated in the Supplemental Box.

Filing date of earlier application (day/month/year)	Number of earlier application	Where earlier application is: national application: country	regional application:* regional Office	international application: receiving Office
item (1) (25.01.99) 25 January 1999	60/117,099	United States of America		
item (2)				
item (3)				

☒ The receiving Office is requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) *(only if the earlier application was filed with the Office which for the purposes of the present international application is the receiving Office)* identified above as item(s): (1)

* *Where the earlier application is an ARIPO application, it is mandatory to indicate in the Supplemental Box at least one country party to the Paris Convention for the Protection of Industrial Property for which that earlier application was filed (Rule 4.10(b)(ii)). See Supplemental Box.*

Box No. VII INTERNATIONAL SEARCHING AUTHORITY

Choice of International Searching Authority (ISA) *(if two or more International Searching Authorities are competent to carry out the international search, indicate the Authority chosen; the two-letter code may be used)* :

ISA/ US

Request to use results of earlier search; reference to that search *(if an earlier search has been carried out by or requested from the International Searching Authority):*

Date *(day/month/year)* Number Country *(or regional Office)*

Box No. VIII CHECK LIST; LANGUAGE OF FILING

This international application contains the following number of sheets:

request	: 4
description (excluding sequence listing part)	: 15
claims	: 3
abstract	: 1
drawings	: 4
sequence listing part of description	: 1
Total number of sheets	: 28

This international application is accompanied by the item(s) marked below:

1. ☒ fee calculation sheet
2. ☐ separate signed power of attorney
3. ☒ copy of general power of attorney; reference number, if any:
4. ☐ statement explaining lack of signature
5. ☐ priority document(s) identified in Box No. VI as item(s):
6. ☐ translation of international application into (language):
7. ☐ separate indications concerning deposited microorganism or other biological material
8. ☒ nucleotide and/or amino acid sequence listing in computer readable form
9. ☐ other *(specify)*:

Figure of the drawings which should accompany the abstract:

Language of filing of the international application: English

Box No. IX SIGNATURE OF APPLICANT OR AGENT

Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the request).

Ellen M. Klann

Ellen M. Klann, Ph.D.
Agent for Applicant

For receiving Office use only

1. Date of actual receipt of the purported international application:
2. Drawings: ☐ received: ☐ not received:
3. Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application:
4. Date of timely receipt of the required corrections under PCT Article 11(2):
5. International Searching Authority (if two or more are competent): ISA/
6. ☐ Transmittal of search copy delayed until search fee is paid.

For International Bureau use only

Date of receipt of the record copy by the International Bureau:

This sheet is not part of and does not count as a sheet of the international application.

PCT

FEE CALCULATION SHEET
Annex to the Request

For receiving Office use only

International application No.

Date stamp of the receiving Office

Applicant's or agent's file reference

Applicant
UNIVERSITY OF MEDICINE AND DENTISTRY OF NEW JERSEY

CALCULATION OF PRESCRIBED FEES

1. TRANSMITTAL FEE . . . . . 240.00 T

2. SEARCH FEE . . . . . 700.00 S

International search to be carried out by US
(If two or more International Searching Authorities are competent in relation to the international application, indicate the name of the Authority which is chosen to carry out the international search.)

3. INTERNATIONAL FEE

Basic Fee
The international application contains 28 sheets.

first 30 sheets 427.00 b1

0 remaining sheets x 10.00 additional amount = 0 b2

Add amounts entered at b1 and b2 and enter total at B . . . . 427.00 B

Designation Fees
The international application contains 5 designations.

5 number of designation fees payable *(maximum 8)* x 92.00 amount of designation fee = 460.00 D

Add amounts entered at B and D and enter total at I . . . . . 887.00 I
(Applicants from certain States are entitled to a reduction of 75% of the international fee. Where the applicant is (or all applicants are) so entitled, the total to be entered at I is 25% of the sum of the amounts entered at B and D.)

4. FEE FOR PRIORITY DOCUMENT *(if applicable)* . . . . . 15.00 P

5. TOTAL FEES PAYABLE . . . . . $1,842.00 TOTAL
Add amounts entered at T, S, I and P, and enter total in the TOTAL box

☐ The designation fees are not paid at this time.

MODE OF PAYMENT

☒ authorization to charge deposit account (see below)
☐ bank draft
☐ coupons
☐ cheque
☐ cash
☐ other *(specify):*
☐ postal money order
☐ revenue stamps

DEPOSIT ACCOUNT AUTHORIZATION *(this mode of payment may not be available at all receiving Offices)*

The RO/ US ☒ is hereby authorized to charge the total fees indicated above to my deposit account.

☐ *(this check-box may be marked only if the conditions for deposit accounts of the receiving Office so permit)* is hereby authorized to charge any deficiency or credit any overpayment in the total fees indicated above to my deposit account.

☐ is hereby authorized to charge the fee for preparation and transmittal of the priority document to the International Bureau of WIPO to my deposit account.

04-1406 — Deposit Account No.

25 January 2000 — Date *(day/month/year)*

Signature Ellen M. Klann, Ph.D.

See Notes to the fee calculation sheet